Editorial Commentary

Guidelines towards comprehensive care in acute pancreatitis

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Acute pancreatitis (AP) represents a common clinical challenge, with increasing incidence globally and with continued rates of high mortality in patients progressing to severe AP despite improvements in the evidence base for early management (1). Timely management from the initial presentation is crucial, underscoring the need for evidence-based guidelines in this field. Tenner *et al.* recently published evidence-based clinical guidelines for the management of AP (2), providing valuable recommendations for clinicians based on a systematic review of current evidence. We would like to add to this important work by offering some additional considerations for optimizing the management of AP.

Pain is the primary presenting clinical symptom of AP, and severe pain has previously been associated with severe disease (3). Pain, being a subjective sensation, may go from mild to intolerable even in the early onset of disease. Yet, the management of pain was not addressed in the current guidelines, likely due to the limited and low-quality evidence available (4). Opioids form the mainstay of pain management in AP (5) and recent randomized controlled trials have suggested improved pain relief with opioids, such as buprenorphine and pentazocine, compared to the non-steroidal anti-inflammatory drug diclofenac (6,7). However, the safety of opioids in AP is continuously being debated. Preclinical data are conflicted regarding the impact of opioids on the severity of AP (8,9), but these studies did not account for potential interspecies differences. Our recent prospective multicenter study with a larger sample size suggested that opioid use was associated with (moderately) severe AP (3). However, this could be confounded by indication. Adding to this, a recent randomized controlled trial found no beneficial effect of peripheral opioid antagonists on severity in AP (10). As such, there is a paucity of recommendations for the management of pain in AP, and further randomized trials are warranted. A further recent multicenter study from our group has shown significant intercontinental differences in the utilization of analgesics, especially opioids, in hospitalized patients with AP (5), underlining the need for streamlining of guidelines in this area of AP. Interdisciplinary European guideline development is currently underway to address the paucity of data and discrepancies in clinical care (11).

The guidelines by Tenner *et al.* (2) advised against the use of antibiotics except in cases of infectious complications, including infected pancreatic necrosis. The authors recognize that antibiotic treatment is not a routine part of AP management and should be reserved for cases with bacterial infection. Several randomized trials and meta-

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analyses have supported this view. However, distinguishing between systemic inflammatory response syndrome and bacterial infection can be challenging in patients with AP. Patients may typically develop signs of infection (e.g., fever, leukocytosis) with high C-reactive protein despite being a sterile inflammation. Procalcitonin measurement may have a potential role in guiding clinicians during this assessment. A recent randomized trial demonstrated the beneficial role of a procalcitonin-guided algorithm for managing antibiotic therapy in patients with AP (12). The study found that this approach reduced antibiotic use without affecting clinical outcomes, suggesting that procalcitonin effectively limited antibiotic administration to the most relevant cases. This has value in keeping the overuse of antibiotics low, avoiding bacterial resistance development, and using the right antibiotic regimens tailored to the needs of the condition.

Tenner *et al.* (2) recommended delayed intervention for pancreatic necrosis, preferably up to 4 weeks, in accordance with the widely used step-up approach for pancreatic walled-off necrosis. Nevertheless, the recent DESTIN trial found that in stable patients with fully encapsulated infected pancreatic necrosis, upfront necrosectomy before four weeks was safe and reduced the need for re-interventions compared to the classical step-up approach (13). In view of this, a case-based approach with tailored indications for endoscopic necrosectomy is warranted in patients with acute necrotic collections in AP.

Finally, the guidelines (2) had no recommendations for a follow-up strategy after an episode of AP. A recent Dutch study with long-term follow-up after necrotizing pancreatitis has shown that a quarter of patients were re-admitted with recurrent pancreatitis, and patients with significant necrosis were at risk of developing exocrine and endocrine deficiency during follow-up (14). Furthermore, emerging evidence has shown that mortality within the first 90 days after discharge was as significant as in-hospital mortality following AP (15). The main cause of death within the first 90 days post-discharge mortality was cardiac failure, which should be noted particularly in the elderly population with AP (16). This contrasted with the more well-documented late complications of AP, such as endo- and exocrine insufficiency and walled-off necrosis. These findings highlight a need for a more comprehensive follow-up strategy and awareness of risk factors for mortality after an episode of AP.

In conclusion, further studies are needed to determine the optimal management of AP, especially on pain management, tailored and appropriate antibiotic treatment, and long-term follow-up. Evidence-based guidelines are crucial for informing clinicians to provide more nuanced and comprehensive care to patients with AP.

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